REMARKS

Entry of the foregoing and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.116, are respectfully requested.

By the foregoing amendment, claims 25 and 39 have been amended to further clarify Applicant's invention. No new matter has been added.

Claims 25-39 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite with regards to the contents of the containers. To expedite prosecution and not acquiesce to the Examiner's rejection, claims 25 and 39 have been amended thus rendering this rejection moot.

Claims 34-38 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking an enabling disclosure. Applicant respectfully traverses this rejection.

The specification does, in fact, teach one skilled in the art how to make and use the claimed composition. The composition of the invention contains MHC molecules which have therapeutic benefits. The detergent extraction methods disclosed, *e.g.*, in Example II, are well-known in the art to selectively extract MHC molecules. See, *e.g.*, specification, p. 3, second paragraph; and Labeta *et al* (1988). *Journal of Immunological Methods* 112, 133-138, cited in the search report of the PCT and of record herein. Such an extract is demonstrated to be effective. See, *e.g.*, Figure 5. Thus, the specification clearly describes how to make the claimed composition.

As a preliminary comment, there is a distinction between "utility" under 35 U.S.C. § 101 and the "how to use" requirement of 35 U.S.C. § 112, first paragraph. A demonstration of the utility of an invention can be satisfied by a showing that the inventive method "works," *e.g.*, in an art-recognized disease model. The model disclosed in the instant specification is an art-recognized one which exhibits a reasonable correlation with cancer. In order to satisfy the "how to use" enablement requirement of 35 U.S.C. § 112, first paragraph, applicant need merely disclose sufficient information that a skilled worker can carry out the inventive method without undue

experimentation. Often, this requires nothing more than disclosing the identity of new compositions, skilled workers being able routinely to determine suitable use details.

In this case, the specification clearly provides more than required to satisfy that requirement. For example, the specification teaches an appropriate treatment regimen. (See, *e.g.*, page 6, line 24 to page 7, line 11). Moreover, the information and data provided in the specification, *e.g.*, showing results using the art-recognized model further guide skilled workers who are familiar with its interpretation. Experiments disclosed in the instant application, for example, involve systemic administration. Moreover, the paper by Ferrero et al. (submitted with the response dated July 8, 1999) shows model results involving treatment using IL-2 which are similar to those of the claimed composition when evaluated in the very same assay. Of course, IL-2 is known to be a general antineoplastic agent against a broad spectrum of tumors. This buttresses the credibility of the specification's disclosure regarding the general applicability of the claimed composition.

Furthermore, the specification clearly teaches a treatment regimen for humans (see, *e.g.*, the final paragraph at p. 6 of the specification). A disclosure of the specific dosages to be administered is not required in order to establish enablement *(Cross v. Iizuka et al*, 224 USPQ 739 (CAFC 1985); *In re Bundy*, 209 USPQ 48 (CCPA 1981); M.P.E.P. § 2164.01 (c), second paragraph).

In addition, applicants submit that the specification is enabling with regard to cross-tissue and cross-species operability. The Examiner has not formally presented evidence or sound scientific reasoning to cast doubt on applicant's assertion that the claimed method is operable in a cross-species or cross-tissue fashion. Nevertheless the Declaration previously submitted with the response dated December 5, 2000 (sections 4-8) clearly shows that MHC preparations from liver exhibit an *in vivo* effect on tumor cells derived from at least two other tissues, *i.e.*, such MHC preparations inhibit the growth of mesothelioma cells, and impair tumor recurrence of colon tumor cells. Furthermore, the specification teaches that MHC from a variety of tissues, sera or cell sources, including red blood cells, can be used to treat cancers which originate from other tissue sources (see, *e.g.*, specification at page 4, lines 9-13). Further, the previously submitted Declaration also shows that MHC preparations from calf inhibit the growth of tumor cells in two other species of animal: mouse and rat (sections 4-8), and that an MHC preparation from calf inhibits the growth of human cells (HT29 human colon carcinoma cells, inoculated into a nude rat)

(sections 4 and 9). Furthermore, the specification teaches that MHC molecules from a variety of species, *e.g.*, bovine red blcod cells, or liver from pig, calf or goat, can be used to treat cancers which originate from heterologous species (see, *e.g.*, specification at page 3, "Summary of the Invention" and original claim 7). In particular, MHC from calf (*e.g.*, Example A, pages 7-8) or goat (*e.g.*, Example B, page 8), or combinations thereof, is shown to inhibit tumors derived from, *e.g.*, rat tissue (Yoshida AH-130 cells). Thus, the specification is enabling with regard to cross-tissue and cross-species operability.

The active principal in the claimed composition is MHC. The Declaration filed with the response dated December 5, 2000 (see section 4, paragraphs 5 and 7) describes at least two types of preparations of extracts: fractions which test positive against, *e.g.*, an MHC-specific monoclonal antibody [MoAb H42A (MHC class II D.B.A. Italia, Segrate)], and fractions which test negative against such monoclonal antibodies, *e.g.*, against MoAb H42A and H58A (MHC class I D.B.A. Italia, Segrate). The latter, control fractions, are referred to in the Declaration as "T-14." The Declaration shows that, in a variety of assays, the former preparations exhibit activity against tumor cells, whereas the control T-14 fractions do not. See, *e.g.*, sections 5-8. These observations support the conclusion that the active principal in the claimed composition is, in fact, MHC.

Furthermore, as discussed in the Reply of July 8, 2000 (page 4, section 2), the claimed composition does not contain components other than MHC which exhibit therapeutic effects. The detergent extraction methods disclosed, *e.g.*, in Example II, are well-known in the art to selectively extract MHC molecules. See, *e.g.*, specification, p. 3, second paragraph; and Labeta *et al* (1988). *Journal of Immunological Methods* 112, 133-138, cited in the search report of the PCT and of record herein. Such an extract is demonstrated to be effective. See, *e.g.*, Figure 5.

Furthermore, section 11 of the Declaration shows that a synthetic peptide from an MHC molecule exhibits antitumor activity which is similar to that of an MHC containing composition of the invention. This supports the conclusion that the active ingredient in the MHC containing composition is, in fact, one or more MHC molecules.

Therefore, in view of the foregoing, applicant respectfully request withdrawal of this rejection.

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney or agent concerning such questions so that prosecution of this application may be expedited.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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Date: March 31, 2003

VERSION WITH MARKINGS TO SHOW CHANGES MADE

25. (Amended) A kit useful for the treatment of a carcinoma in a patient, comprising at least two containers, each comprising an extract from an animal tissue, serum or cell source ~~different from that of the other container,~~ wherein said extracts

a) comprise allogeneic or xenogeneic MHC molecules;

b) are prepared by a) homogenizing the tissue, serum or cell source in the presence of NP40, or b) treating said source with an acid, or c) treating said source with a proteolytic enzyme; and

c) are each effective to reduce the number of tumor cells in the patient compared to the number of tumor cells if the patient is not so treated,

wherein the source of the extract in one container is from i) a tissue, serum or cell different from the tissue, serum or cell for the other container, and from the same animal ii) a tissue, serum or cell from a different animal of the same species as the animal source for the other container or iii) a tissue, serum or cell from an animal from a different species as the animal source for the other container.

39. (Amended) A kit useful for the treatment of a carcinoma in a patient, comprising at least two containers, each comprising an amount of MHC molecules which may be found in an animal tissue, serum or cell source ~~different from that of the other container~~, wherein said extracts

a) comprise allogeneic or xenogeneic MHC molecules;

b) are prepared by a) homogenizing the tissue, serum or cell source in the presence of NP40, or b) treating said source with an acid, or c) treating said source with a proteolytic enzyme; and

c) are each effective to reduce the number of tumor cells in the patient compared to the number of tumor cells if the patient is not so treated,

wherein the source of the extract in one container is from i) a tissue, serum or cell different from the tissue, serum or cell for the other container, and from the same animal; ii) a tissue, serum or cell from a different animal of the same species as the animal source for the other container; or iii) a

tissue, serum or cell from an animal from a different species as the animal source for the other container.